June 19, 1954

Dr. William Cherry
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Dear Bill:

I was very happy to hear from you about your work with Bacillus. I had seen the Manninger-Tomscik contributions, but found them rather unconvincing. There was a hint of your new stuff on a reprint postcard from Brown (I think), and I had been waiting to hear some details of it.

I will try to answer your questions about the Salmonella system. Some of the points are taken up rather obliquely in the various papers (see also Zinder, Cold Spr Harb Symp. Vol 18), but some of the findings have not been published in detail.

Q. Inactivation by DNAse? A. No effect of the enzyme. The idea that the phage particle carries "DNA" is hypothetical, by analogy with the pneumococcus story. To my mind "DNA" is another term for "chromosome fragment"; whether DNA is absolutely all that is relevant has not, to my mind, been finally settled.

Q. Phage or something else in lysate. A. The genetic activity is carried by particles (sedimentable at high speed) which are indistinguishable from phage in the following respects: size (filtration)(sedimentation); tolerance to heat; tolerance to certain disinfectants; tolerance to ultrasonic disruption; neutralization by anti-phage serum; absorption by live or killed susceptible bacteria (and non-absorption by rough or other serotypes). The ratio of activity to phage count is constant for different lysates. All this would show that the active particle is superficially similar to phage, but does not exclude that the internal contents of the particle might be different. However, Under conditions of low multiplicity of infection, there is a definite correlation between transduction and lysogenization, so that the particle carrying the activity must also carry phage activity. (Of course most phage particles are transductively inactive).

Q. Separation of phage from genetic activity. A. Of course, not every genetic effect of phage is transduction. Most phage particles are inactive (distinction from the diphtheria toxigenicity effect, e.g.). Also, the activity of a given lysate depends completely on the bacterial host. We have not found any method of depriving a phage prep'n of its transducing competence (except of course by growing it on a new host) without impairing its lytic activity at the same time. With ultra-violet light, however, the lytic activity is destroyed (presumably by lethal mutations in the phage)

much more rapidly than transductive competence. With UV'd phage, therefore, one can get transduction without lysogenization. This also happens fairly often with maladaptive phage-bacterium combinations , e.g. typhimurium phage + paratyphiB.

I would like to hear more of your findings/ I am afraid I did not fully assimilate your letter. Do I understand that you propagate phage on a non-motile B. anthracis and get lysates that will confer motility on the same or related anthrax strains? This does notsuggest transduction in the same sense as in Salmonella. (The DNAse effect might mean that the genetic material is more accessible, perhaps nearer the outside of the phage particle). It might ~~Do this not~~ be closer to the diphtheria story.

Of course your confidences on this story will be fully respected-- I trust you will let me know when they can be relaxed.

With best regards,

Yours sincerely,

Joshua Lederberg
Professor of Genetics